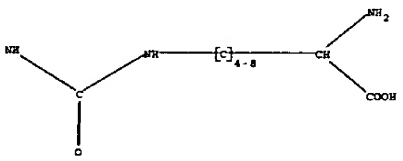
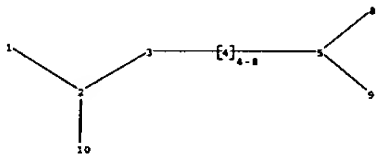
STN Structure : 09944209.str





chain nodes :
1 2 3 4 5 8 9 10
chain bonds :
1-2 2-3 2-10 3-4 4-5 5-8 5-9
exact/norm bonds :
1-2 2-3 2-10 3-4 5-8
exact bonds :
4-5 5-9

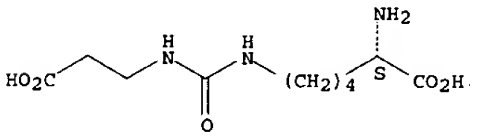
Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 8:CLASS 9:CLASS 10:CLASS

L6 ANSWER 26 OF 46 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:172202 CAPLUS
DOCUMENT NUMBER: 106:172202
TITLE: Limitations of N-hydroxysuccinimide esters in affinity chromatography and protein immobilization
AUTHOR(S): Wilchek, Meir; Miron, Talia
CORPORATE SOURCE: Dep. Biophys., Weizmann Inst. Sci., Rehovot, 76100, Israel
SOURCE: Biochemistry (1987), 26(8), 2155-61
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The carbodiimide-mediated reaction of N-hydroxysuccinimide with carboxyl groups immobilized via addn. of aminocaproic acid to hydroxyl-contg. polymers (such as Sepharose or Trisacryl) leads to an undesirable side reaction in high yields, the product of which interferes with the application of such columns for further affinity-based purifn. In addn. to the desired N-hydroxysuccinimide ester, a bis(N-hydroxysuccinimide) deriv. of .beta.-alanine [namely, N-[(succinimidooxy)carbonyl]-.beta.-alanine N-hydroxysuccinimide ester] is produced that reacts subsequently with the hydroxyl group of the polymer via ester and carbamate bonds. These .beta.-alanine derivs. are formed upon interaction of dicyclohexylcarbodiimide with 3 equiv of N-hydroxysuccinimide followed by a Lossen rearrangement. The amt. of .beta.-alanine thus coupled is very high compared to the no. of carboxyl groups present on the resin. The .beta.-alanine bound through the ester bond comprises about 90% of the .beta.-alanine bound. Alk. treatment of the ester-bonded .beta.-alanine-contg. polymers (prior to coupling of amino-contg. ligands) causes a rearrangement yielding .beta.-alanine with a free carboxyl group coupled through a stable carbamate linkage. After coupling of amino-contg. ligands, the rearrangement cannot occur, and the .beta.-alanine-linked ligand leaks from the polymer via hydrolysis of the ester bond. The newly formed carboxyl groups (derived from the rearrangement) can be used to prep. active esters. In view of the above, methods were developed for the prepn. of nitrophenyl esters as well as N-hydroxysuccinimide esters free of unstable .beta.-alanine derivs. on polymers contg. hydroxyl groups. Upon coupling with amino-contg. ligands, these esters yield resins bearing chem. stable bonds.

IT 107037-32-1
RL: FORM (Formation, nonpreparative)
(formation of, from lysine-immobilized agarose by alkali hydrolysis)
RN 107037-32-1 CAPLUS
CN L-Lysine, N6-[[(2-carboxyethyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:324507 CAPLUS
DOCUMENT NUMBER: 122:106538
TITLE: Preparation of peptide urethane and urea derivatives that induce cytokine production
INVENTOR(S): Ayral-Kaloustian, Semiramis; Schow, Steven R.; Du, Mila T.; Gibbons, James J., Jr.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 25 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

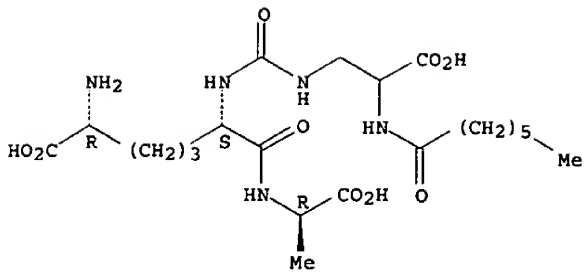
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5312831	A	19940517	US 1993-63174	19930512
US 5545662	A	19960813	US 1994-213303	19940314
EP 652228	A1	19950510	EP 1994-106123	19940420
EP 652228	B1	19961023		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 144533	E	19961115	AT 1994-106123	19940420
ES 2094004	T3	19970101	ES 1994-106123	19940420
SK 281120	B6	20001211	SK 1994-491	19940428
HU 67038	A2	19950130	HU 1994-1444	19940506
HU 219768	B	20010730		
JP 07179414	A2	19950718	JP 1994-119532	19940509
IL 109602	A1	20000601	IL 1994-109602	19940509
CA 2123261	AA	19941113	CA 1994-2123261	19940510
FI 9402186	A	19941113	FI 1994-2186	19940511
NO 9401786	A	19941114	NO 1994-1786	19940511
AU 9463043	A1	19941117	AU 1994-63043	19940511
AU 669064	B2	19960523		
ZA 9403266	A	19950112	ZA 1994-3266	19940511
RU 2135515	C1	19990827	RU 1994-16389	19940511
PL 179984	B1	20001130	PL 1994-303396	19940511
CN 1100413	A	19950322	CN 1994-105671	19940512
TW 380129	B	20000121	TW 1994-83107431	19940813
US 5602275	A	19970211	US 1995-449878	19950525
US 5616612	A	19970401	US 1995-451099	19950525
US 5633280	A	19970527	US 1995-451085	19950525
US 5658945	A	19970819	US 1995-449968	19950525

PRIORITY APPLN. INFO.: US 1993-63174 A3 19930512
US 1994-213303 A3 19940314
OTHER SOURCE(S): MARPAT 122:106538

AB Title compds. [I; R1, R3, Ra = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, vinyl, acetylene, amino, acylamino, aryl, aralkyl, aryloxy, heterocyclyl, etc.; R2, Rb, Rc = (protected) carboxy, carboxylalkyl, carboxamide; X = O, S; R4 = H, protecting group], were prepd. Thus, [R-(R*,R*)]-N-(R)-6-carboxy-N2-[[2-carboxy-1-methyl-2-[(1-oxoheptyl)amino]ethoxy]carbonyl]lysyl-D-alanine (soln. phase prepn. given) at 0.1 mg/kg s.c. in mice induced 4802 U/mL of IL-6. I may be useful in the treatment of cancer, AIDS, aplastic anemia, myelodysplastic syndrome, infectious disease, and in the enhancement of immune response.

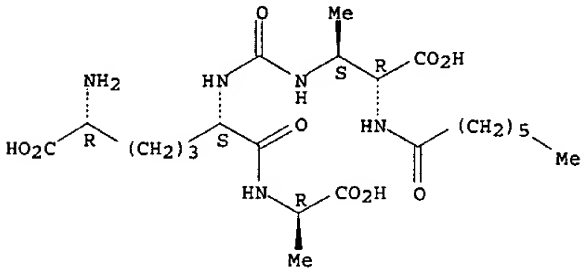
IT **160578-77-8P 160578-78-9P 160705-80-6P**
160705-89-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for induction of cytokine prodn.)
RN 160578-77-8 CAPLUS
CN D-Alanine, N-[(R)-6-carboxy-N2-[[[2-carboxy-2-[(1-oxoheptyl)amino]ethyl]amino]carbonyl]-L-lysyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



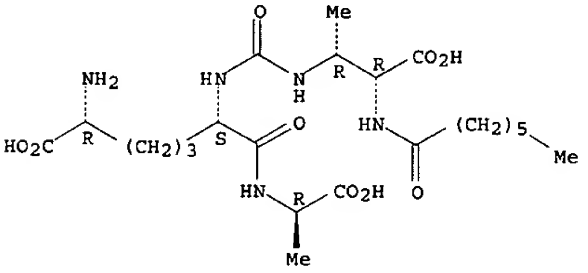
RN 160578-78-9 CAPLUS
CN D-Alanine, N-[(R)-6-carboxy-N2-[[[2-carboxy-1-methyl-2-[(1-oxoheptyl)amino]ethyl]amino]carbonyl]-L-lysyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



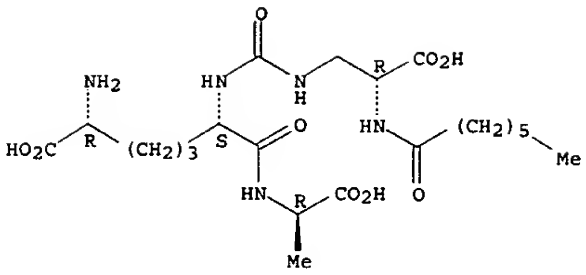
RN 160705-80-6 CAPLUS
CN D-Alanine, N-[(R)-6-carboxy-N2-[[[2-carboxy-1-methyl-2-[(1-oxoheptyl)amino]ethyl]amino]carbonyl]-L-lysyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 160705-89-5 CAPLUS
CN D-Alanine, N-[(R)-6-carboxy-N2-[[[2-carboxy-2-[(1-oxoheptyl)amino]ethyl]amino]carbonyl]-L-lysyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


O
NH2
HN
N
H
R
CO2H
HO2C
R
(CH2)3
S
O
HN
(CH2)5
Me
HN
R
CO2H
O
Me

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:135731 CAPLUS
DOCUMENT NUMBER: 110:135731
TITLE: Preparation and testing of peptidylaminodiols as renin inhibitors
INVENTOR(S): Fung, Anthony K. L.; Kempf, Dale John; Luly, Jay Richard; Rosenberg, Saul Howard; Plattner, Jacob John
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8805050	A1	19880714	WO 1987-US3376	19871222
W: AU, DK, JP, KR				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
IL 97441	A1	19920906	IL 1987-97441	19870112
US 5032577	A	19910716	US 1987-132356	19871218
AU 8811580	A1	19880727	AU 1988-11580	19871222
AU 609774	B2	19910509		
EP 295294	A1	19881221	EP 1988-900918	19871222
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 01502514	T2	19890831	JP 1988-501082	19871222
IL 84945	A1	19920216	IL 1987-84945	19871225
US 4845079	A	19890704	US 1988-217106	19880711
DK 8804834	A	19880830	DK 1988-4834	19880830
CA 1307289	A2	19920908	CA 1991-615975	19910108
AU 9170281	A1	19910418	AU 1991-70281	19910205
AU 638093	B2	19930617		
US 5091575	A	19920225	US 1991-713644	19910610
US 5214129	A	19930525	US 1991-793773	19911118

PRIORITY APPLN. INFO.:

US 1986-943567	19861231
US 1987-132356	19871218
US 1985-693951	19850123
US 1986-818714	19860116
US 1986-818715	19860116
US 1986-818734	19860116
US 1986-895009	19860807
IL 1987-81234	19870112
CA 1987-527514	19870116
WO 1987-US3376	19871222
US 1988-217106	19880711
US 1989-327467	19890322
US 1991-713644	19910610

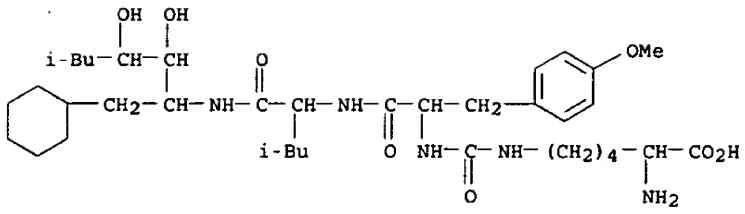
OTHER SOURCE(S): MARPAT 110:135731

AB ACHR1-W-U-CHR3CONHCHR4CR5R8CR6R7R9 [I; A = (un)substituted amino, acylamino, etc.; W = CO, CHOH; U = CH2, NR2; R1 = alkyl, cycloalkylmethyl, (substituted) PhCH2, anilino, thiophenoxy, etc.; R2, R7 = H, alkyl; R3 = alkyl, alkenyl, alkoxyalkoxyalkyl, PhCH2, heterocyclylmethyl; R4 = alkyl, cycloalkylmethyl, PhCH2; R5 = H, CH2:CH, HCO, HOCH2; R6 = H, alkyl, CH2:CH, arylalkyl; R8, R9 = OH, NH2}, useful as renin inhibitors, were prepd. 2S-tert-Butyloxycarbonylamino-1-cyclohexylbut-3-ene (prepn. given) was deprotected with HCl/MeOH and coupled with BOC-Phe-Ala-OH (BOC = CO2CMe3), using iso-Bu chloroformate and N-methylmorpholine in THF/DMF at -13.degree.. the product was treated with OsO4/N-methylmorpholine N-oxide in THF to give 3S-N-(tert-butoxycarbonylphenylalanylalanylamino)-4-cyclohexyl-1,2(R,S)-dihydroxybutane. I inhibited renin with IC50's of 0.3-4000 nM.

IT **119609-96-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)

RN 119609-96-0 CAPLUS

CN L-Leucinamide, N-[[(5-amino-5-carboxypentyl)amino]carbonyl]-O-methyl-L-tyrosyl-N-{1-(cyclohexylmethyl)-2,3-dihydroxy-5-methylhexyl}-, [1(S),2[1S-(1R*,2S*,3R*)]]- (9CI) (CA INDEX NAME)



L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:3105 CAPLUS
DOCUMENT NUMBER: 102:3105
TITLE: Protection by D-amino acids against growth inhibition and lysis caused by .beta.-lactam antibiotics
AUTHOR(S): Tuomanen, Elaine; Tomasz, Alexander
CORPORATE SOURCE: Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Antimicrob. Agents Chemother. (1984), 26(3), 414-16
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

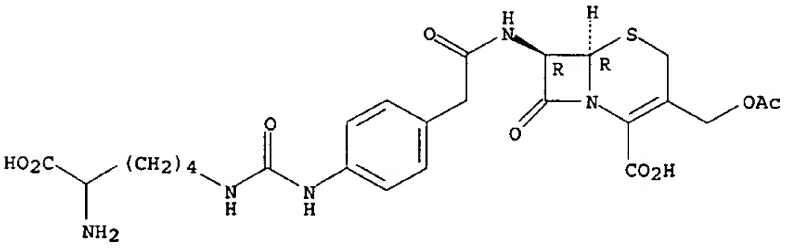
AB D-Isomers of several amino acids completely protected growing cultures of Escherichia coli against all antibacterial effects of .beta.-lactam antibiotics up to 2-3-fold the min. inhibitory concns. of the antibiotics. L-Isomers of amino acids were ineffective. Protection depended on the concn. and time of addn. of the D-amino acids. This appears to be the first demonstration of natural products capable of reversing the antibacterial effects of .beta.-lactam antibiotics.

IT **93265-85-1**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antibacterial activity of, D-amino acids protection against)

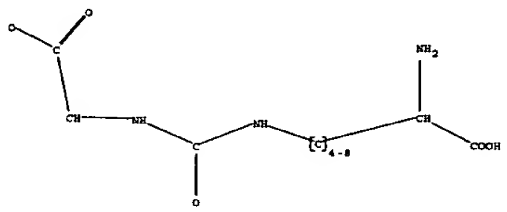
RN 93265-85-1 CAPLUS

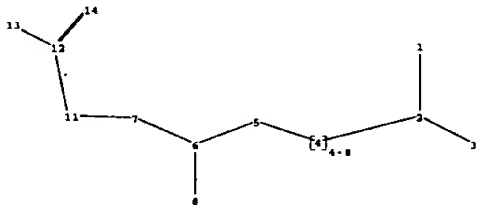
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-7-[[[4-[[[(5-amino-5-carboxypentyl)amino]carbonyl]amino]phenyl]acetyl]amino]-8-oxo-, [6R-(6.alpha.,7.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



STN Structure : 09944209.str





chain nodes :
1 2 3 4 5 6 7 8 11 12 13 14
chain bonds :
1-2 2-3 2-4 4-5 5-6 6-7 6-8 7-11 11-12 12-13 12-14
exact/norm bonds :
1-2 4-5 5-6 6-7 6-8 7-11 12-13 12-14
exact bonds :
2-3 2-4 11-12

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 11:CLASS 12:CLASS
13:CLASS 14:CLASS

1190-49-4

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:758638 CAPLUS
DOCUMENT NUMBER: 123:144647
TITLE: Ureas derived from .alpha.,.omega.-diamino acids and process for their preparation.
INVENTOR(S): Callens, Roland; Blondeel, Georges; Anteunis, Marc; Becu, Frank
PATENT ASSIGNEE(S): Solvay et Cie., Belg.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 629612	A1	19941221	EP 1994-201643	19940609
EP 629612	B1	19991201		
R: AT, BE, CH, DE, ES, FR, GB, IE, IT, LI, NL, SE				
BE 1007183	A3	19950418	BE 1993-621	19930618
EP 922696	A2	19990616	EP 1999-103523	19940609
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE				
AT 187162	E	19991215	AT 1994-201643	19940609
ES 2141795	T3	20000401	ES 1994-201643	19940609
CA 2125638	AA	19941219	CA 1994-2125638	19940610
IL 109978	A1	19991028	IL 1994-109978	19940610
AU 9464781	A1	19941222	AU 1994-64781	19940617
AU 685794	B2	19980129		
HU 71414	A2	19951128	HU 1994-1821	19940617
JP 07048356	A2	19950221	JP 1994-137117	19940620
US 6060586	A	20000509	US 1997-985658	19970617
US 6310178	B1	20011030	US 2000-502561	20000211

PRIORITY APPLN. INFO.:
BE 1993-621 A 19930618
EP 1994-201643 A3 19940609
US 1994-257292 B1 19940609
US 1997-985658 A3 19970617

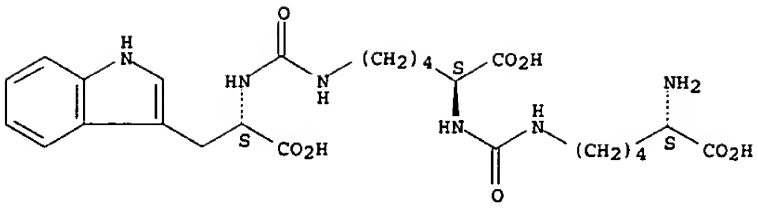
OTHER SOURCE(S): CASREACT 123:144647; MARPAT 123:144647

AB Ureas derived from .alpha.,.omega.-diamino acids are prepd. by reaction of N.omega.-(aryloxycarbonyl) diamino acid derivs. with compds. contg. a free amino group, in a basic medium. The method includes prepn. of acyclic ureas I [A = (un)substituted linear carbon chain; R = amino acid or peptide residue], cyclic ureas II, and cyclic urea-derived peptides III. The latter are analogs of TRH (TSH releasing hormone) with improved resistance to proteolytic digestion (no data). For example, reaction of 25 mmol tryptophan with 5 mmol N.epsilon.-(phenyloxycarbonyl)lysine in H2O contg. LiOH at 75.degree. gave 880 mg N.epsilon.-(N.alpha.-tryptophancarbonyl)lysine plus 76 mg of a tripeptide byproduct. The method gives improved chem. yield without racemization. Alternatively, L-N.gamma.-(phenyloxycarbonyl)diaminobutyric acid was cyclized by Et3N in refluxing aq. MeOH to give L-2-oxohexahydropyrimidine-4-carboxylic acid (IV) in 95% yield. IV was coupled with H-His-Pro-NH2.2HBr by the mixed anhydride method to give the corresponding III.

IT **166961-67-7P**
RL: BYP (Byproduct); PREP (Preparation)
(byproduct; prepn. of ureas derived from .alpha.,.omega.-diamino acids)

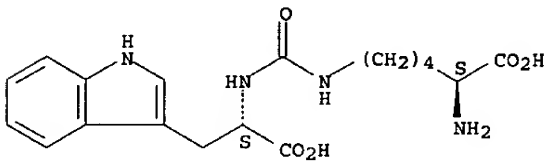
RN 166961-67-7 CAPLUS
CN 2,4,10,12-Tetraazaheptadecane-1,9,17-tricarboxylic acid, 17-amino-1-(1H-indol-3-ylmethyl)-3,11-dioxo-, [1S-(1R*,9R*,17R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



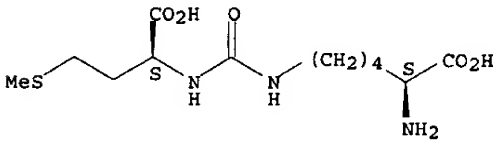
IT **166961-66-6P 166961-68-8P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of ureas derived from .alpha.,.omega.-diamino acids)
RN 166961-66-6 CAPLUS
CN L-Tryptophan, N-[[(5-amino-5-carboxypentyl)amino]carbonyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

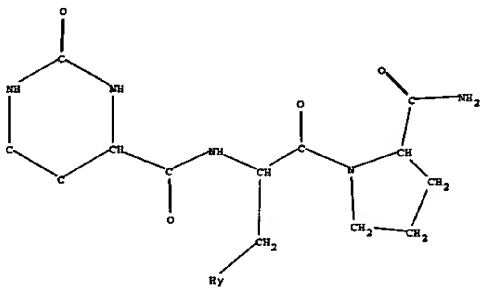


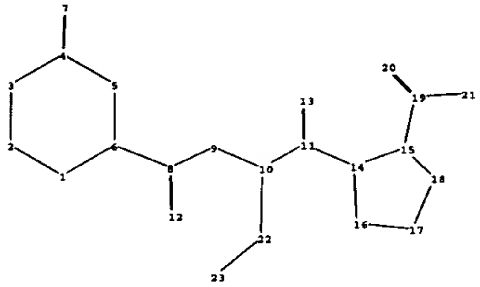
RN 166961-68-8 CAPLUS
CN L-Lysine, N6-[[[1-carboxy-3-(methylthio)propyl]amino]carbonyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



STN Structure : 09944209.str





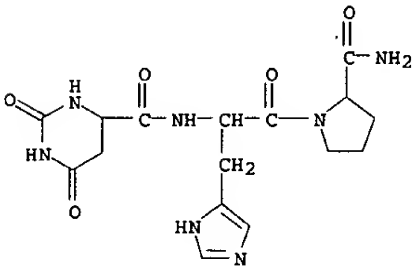
chain nodes :
7 8 9 10 11 12 13 19 20 21 22 23
ring nodes :
1 2 3 4 5 6 14 15 16 17 18
chain bonds :
4-7 6-8 8-9 8-12 9-10 10-11 10-22 11-13 11-14 15-19 19-20 19-21 22-23
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 14-15 14-16 15-18 16-17 17-18
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 8-9 8-12 9-10 11-13 11-14 14-15 14-16 15-18
16-17 17-18 19-20 19-21 22-23
exact bonds :
6-8 10-11 10-22 15-19

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom

L11 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:426820 CAPLUS
DOCUMENT NUMBER: 135:147620
TITLE: A thyroliberin analogue reverses disturbances of behaviour and brain biogenic amine levels in antenatally hypoxised rats
AUTHOR(S): Semenova, Tatiana; Anoshkina, Irina; Fast, Alla; Klusa, Vija
CORPORATE SOURCE: Institute of Cell Biophysics, Russian Academy of Sciences, Oblast, 142 292, Russia
SOURCE: Proc. Latv. Acad. Sci., Sect. B (2001), 55(1), 23-29
CODEN: PLABFE; ISSN: 1407-009X
PUBLISHER: Latvian Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dihydroorotyl-histidyl-prolinamide (IOS-1.1101), a TSH-releasing hormone (TRH, or thyroliberin) analog, injected i.p. at a dose of 100 .mu.g.kg-1 in adult male rats which were hypoxised antenatally (on days 14-16 of their mothers' pregnancy), reversed the hypoxia-induced disturbances in attention, exploratory, emotional, and learning abilities, as well as in the brain noradrenaline and serotonin concns. The data obtained showed IOS-1.1101 to be a strong corrector of antenatal hypoxia-induced disturbances in CNS activity which can be manifested during rat adulthood. These anti-neurodeficit properties indicate the usefulness of this compd. in mentally retarded human newborns exposed to hypoxia during their fetal period.

IT **59760-05-3**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(thyroliberin analog reverses disturbances of behavior and brain biogenic amine levels in antenatally hypoxised rats)
RN 59760-05-3 CAPLUS
CN L-Prolinamide, N-[[(4S)-hexahydro-2,6-dioxo-4-pyrimidinyl]carbonyl]-L-histidyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:758638 CAPLUS
DOCUMENT NUMBER: 123:144647
TITLE: Ureas derived from .alpha.,.omega.-diamino acids and process for their preparation.
INVENTOR(S): Callens, Roland; Blondeel, Georges; Anteunis, Marc; Becu, Frank
PATENT ASSIGNEE(S): Solvay et Cie., Belg.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 629612	A1	19941221	EP 1994-201643	19940609

EP 629612	B1	19991201			
R: AT, BE, CH, DE, ES, FR, GB, IE, IT, LI, NL, SE					
BE 1007183	A3	19950418	BE 1993-621		19930618
EP 922696	A2	19990616	EP 1999-103523		19940609
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE					
AT 187162	E	19991215	AT 1994-201643		19940609
ES 2141795	T3	20000401	ES 1994-201643		19940609
CA 2125638	AA	19941219	CA 1994-2125638		19940610
IL 109978	A1	19991028	IL 1994-109978		19940610
AU 9464781	A1	19941222	AU 1994-64781		19940617
AU 685794	B2	19980129			
HU 71414	A2	19951128	HU 1994-1821		19940617
JP 07048356	A2	19950221	JP 1994-137117		19940620
US 6060586	A	20000509	US 1997-985658		19970617
US 6310178	B1	20011030	US 2000-502561		20000211
PRIORITY APPLN. INFO.:			BE 1993-621	A	19930618
			EP 1994-201643	A3	19940609
			US 1994-257292	B1	19940609
			US 1997-985658	A3	19970617

OTHER SOURCE(S): CASREACT 123:144647; MARPAT 123:144647

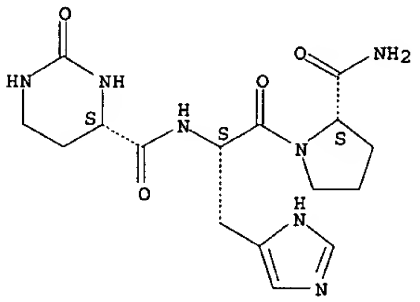
AB Ureas derived from .alpha.,.omega.-diamino acids are prepd. by reaction of N.omega.-(aryloxycarbonyl) diamino acid derivs. with compds. contg. a free amino group, in a basic medium. The method includes prepn. of acyclic ureas I [A = (un)substituted linear carbon chain; R = amino acid or peptide residue), cyclic ureas II, and cyclic urea-derived peptides III. The latter are analogs of TRH (TSH releasing hormone) with improved resistance to proteolytic digestion (no data). For example, reaction of 25 mmol tryptophan with 5 mmol N.epsilon.-(phenyloxycarbonyl)lysine in H2O contg. LiOH at 75.degree. gave 880 mg N.epsilon.-(N.alpha.-tryptophancarbonyl)lysine plus 76 mg of a tripeptide byproduct. The method gives improved chem. yield without racemization. Alternatively, L-N.gamma.-(phenyloxycarbonyl)diaminobutyric acid was cyclized by Et3N in refluxing aq. MeOH to give L-2-oxohexahydropyrimidine-4-carboxylic acid (IV) in 95% yield. IV was coupled with H-His-Pro-NH2.2HBr by the mixed anhydride method to give the corresponding III.

IT **166961-72-4P**
RL: BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRH analog; prepn. of ureas derived from .alpha.,.omega.-diamino acids)

RN 166961-72-4 CAPLUS

CN L-Prolinamide, N-[(hexahydro-2-oxo-4-pyrimidinyl)carbonyl]-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:498021 CAPLUS

DOCUMENT NUMBER: 113:98021

TITLE: Synthesis and central nervous system actions of thyrotropin-releasing hormone analog containing a dihydroorotic acid moiety

AUTHOR(S): Suzuki, Mamoru; Sugano, Hiroshi; Matsumoto, Kazuo; Yamamura, Michio; Ishida, Ryuichi

CORPORATE SOURCE: Res. Lab. Appl. Biochem., Tanabe Seiyaku Company Ltd.,

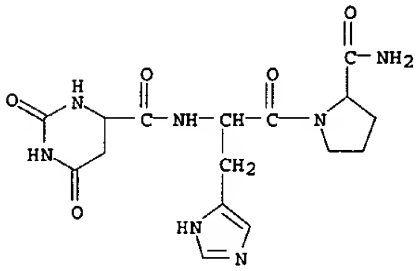
Osaka, 532, Japan
SOURCE: J. Med. Chem. (1990), 33(8), 2130-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:98021

AB A series of TSH-releasing hormone (TRH) analogs in which the pyroglutamic acid residue was replaced by (S)-4,5-dihydroorotic acid and related derivs. were prepd. Their central nervous system actions based on spontaneous locomotor activity, antagonistic effect on reserpine-induced hypothermia, and antagonistic effect on pentobarbital anesthesia were evaluated and the structure-activity relationships are discussed. Of these, analog I showed the most potent activities, which were 30-90 times greater than those of TRH. Moreover, the TSH-releasing activity of I was about 50 times weaker than that of TRH.

IT 59760-05-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and central nervous system activity of)

RN 59760-05-3 CAPLUS

CN L-Prolinamide, N-[[(4S)-hexahydro-2,6-dioxo-4-pyrimidinyl]carbonyl]-L-histidyl- (9CI) (CA INDEX NAME)



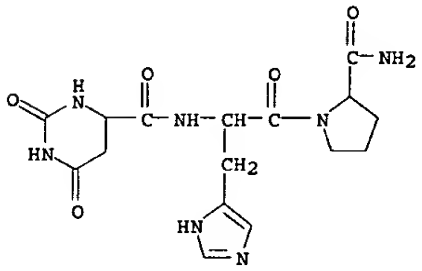
L11 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:527698 CAPLUS
DOCUMENT NUMBER: 95:127698
TITLE: Degradation of TRF and TRF analogs by brain and serum enzymes
AUTHOR(S): Bauer, Karl; Kleinkauf, Horst; Flohe, Leopold
CORPORATE SOURCE: Max-Volmer-Inst., Tech. Univ. Berlin, Berlin, D-1000/10, Fed. Rep. Ger.
SOURCE: Struct. Act. Nat. Pept., Proc. Fall Meet. Ges. Biol. Chem. (1981), Meeting Date 1979, 437-47. Editor(s): Voelter, Wolfgang; Weitzel, Guenther. de Gruyter: Berlin, Fed. Rep. Ger.
CODEN: 45VYAS
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Neither pyroglutamate aminopeptidase (I) nor thyrotropin-releasing factor (TRF)-degrading serum enzyme (II) degraded TRF analogs in which the pyroglutamyl was replaced by a 6-membered ring. II catalyzed the degrdn. of a thiazolidinone TRF deriv., but not that of the corresponding imidazolidinone analog. By contrast, I hydrolyzed the imidazolidinone deriv. more efficiently than TRF itself. All TRF analogs contg. the structure -His-Pro-NH2 were deaminated by post-proline-cleaving enzyme (III). TRF, the 5-membered-ring analogs of TRF, and orotyl-contg. TRF analogs were degraded at comparable rates, whereas thiomorpholine-contg. analogs of TRF were deaminated more slowly. Although orotyl-His-Pro-NH2 was deaminated more rapidly than TRF itself, orotyl-His-Pro-NHCH3 was not degraded by III. Thus, the affinity of substrates for these enzymes is influenced by structural elements remote from the scissile peptide bond.

IT 79056-84-1
RL: RCT (Reactant)
(reaction of, with brain and serum enzymes, releasing factor degrdn. in relation to)

RN 79056-84-1 CAPLUS

CN L-Prolinamide, N-[(hexahydro-2,6-dioxo-4-pyrimidinyl)carbonyl]-L-histidyl- (9CI) (CA INDEX NAME)



5,151,497

L11 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:447062 CAPLUS
DOCUMENT NUMBER: 85:47062
TITLE: Dipeptide derivatives
INVENTOR(S): Schwertner, Eberhard; Herrling, Siegfried
PATENT ASSIGNEE(S): Chemie Gruenenthal G.m.b.H., Ger.
SOURCE: Ger. Offen., 21 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2449167	A1	19760422	DE 1974-2449167	19741016
DE 2449167	C2	19840524		
US 3876872	A	19750408	US 1971-189252	19711014
ZA 7206620	A	19730725	ZA 1972-6620	19720927
AU 7247113	A1	19740404	AU 1972-47113	19720927
IT 987571	A	19750320	IT 1972-29950	19720930
GB 1413822	A	19751112	GB 1972-45834	19721004
GB 1413823	A	19751112	GB 1975-27168	19721004
DE 2249860	A1	19730530	DE 1972-2249860	19721011
FR 2187155	A5	19740111	FR 1972-36439	19721013
JP 48061888	A2	19730829	JP 1972-103166	19721014
AT 348694	B	19790226	AT 1975-6044	19750804
NL 7510288	A	19760421	NL 1975-10288	19750901
NL 183764	B	19880816		
NL 183764	C	19890116		
SE 408300	C	19790913	SE 1975-9703	19750901
SE 408300	B	19790605		
ZA 7505956	A	19760825	ZA 1975-5956	19750918
JP 51065775	A2	19760607	JP 1975-122966	19751014
JP 60009518	B4	19850311		
ES 441788	A1	19770616	ES 1975-441788	19751014
DK 7504637	A	19760417	DK 1975-4637	19751015
DK 149063	B	19860106		
DK 149063	C	19860616		
FR 2287916	A1	19760514	FR 1975-31599	19751015
CA 1056818	A1	19790619	CA 1975-237665	19751015
CH 616913	A	19800430	CH 1975-13382	19751015
BE 834590	A1	19760416	BE 1975-161007	19751016
US 4045556	A	19770830	US 1975-622804	19751016
AT 7707218	A	19790615	AT 1977-7218	19771010
AT 354657	B	19790125		
AT 7803009	A	19800515	AT 1978-3009	19780426
AT 360186	B	19801229		

PRIORITY APPLN. INFO.:	US 1971-189252	19711014
	DE 1974-2449167	19741016
	DE 1975-2527723	19750621
	AT 1975-6044	19750804

AB Treatment of L-histidine with the N-hydroxysuccinimide ester of

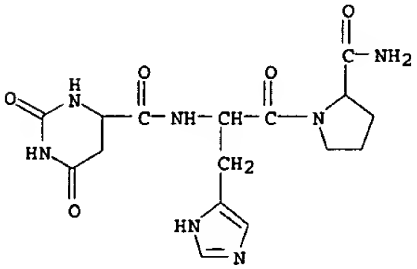
N-benzyloxycarbonyl-L-2-oxoimidazolidine-4-carboxylic acid followed by L-prolinamide and debenzyloxycarbonylation gave L-2-oxoimidazolidine-4-carbonyl-L-histidyl-L-prolinamide. Condensation of orotic acid or L-5-oxothiomorpholine-3-carboxylic acid with His-Pro-NH2.2HBr gave orotyl- or L-5-oxothiomorpholine-3-carbonyl-L-histidyl-L-prolinamide.

IT **59760-05-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 59760-05-3 CAPLUS

CN L-Prolinamide, N-[[(4S)-hexahydro-2,6-dioxo-4-pyrimidinyl]carbonyl]-L-histidyl- (9CI) (CA INDEX NAME)



L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 24305-27-9 REGISTRY
CN L-Prolinamide, 5-oxo-L-prolyl-L-histidyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Thyrotropin-releasing factor (8CI)
OTHER NAMES:
CN (Pyro)-L-glutamic acid-L-histidine-L-proline-NH2
CN Antepan
CN FDA 1725
CN L-Pyroglutamyl-L-histidyl-L-prolinamide
CN L-Pyroglutamyl-L-histidyl-L-proline amide
CN Lopremone
CN Prem
CN Protirelin
CN Relefact TRH
CN Rifathyroin
CN Rifotironin
CN Ro 8-6270/9
CN Synthetic thyrotropin-releasing factor
CN Synthetic thyrotropin-releasing hormone
CN Synthetic TRF
CN Synthetic TRH
CN Synthetic TSH-releasing factor
CN Synthetic TSH-releasing hormone
CN Thyrefact
CN Thyroid releasing hormone
CN Thyroid-stimulating hormone-releasing factor
CN **Thyroliberin**
CN Thyrotropic hormone-releasing factor
CN Thyrotropic hormone-releasing hormone
CN Thyrotropic releasing hormone
CN Thyrotropic-releasing factor
CN Thyrotropin-releasing hormone
CN TRF
CN TRH
CN TSH-releasing factor
CN TSH-releasing hormone
CN TSH-RF
FS STEREOSEARCH
DR 9015-91-2, 22365-02-2, 22365-17-9, 77666-61-6, 39422-15-6
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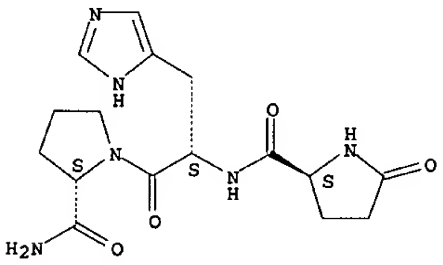
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7808 REFERENCES IN FILE CA (1967 TO DATE)